Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study

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Summary

Background **Information about the variation in the risk for venous thromboembolism (VTE) and in prophylaxis practices around the world is scarce. The ENDORSE (Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care Setting) study is a multinational cross-sectional survey designed to assess the prevalence of VTE risk in the acute hospital care setting, and to determine the proportion of at-risk patients who receive effective prophylaxis.**

Methods **All hospital inpatients aged 40 years or over admitted to a medical ward, or those aged 18 years or over admitted to a surgical ward, in 358 hospitals across 32 countries were assessed for risk of VTE on the basis of hospital chart review. The 2004 American College of Chest Physicians (ACCP) evidence-based consensus guidelines were used to assess VTE risk and to determine whether patients were receiving recommended prophylaxis.**

Findings **68 183 patients were enrolled; 30 827 (45%) were categorised as surgical, and 37 356 (55%) as medical. On the basis of ACCP criteria, 35 329 (51·8%; 95% CI 51·4–52·2; between-country range 35·6–72·6) patients were judged to be at risk for VTE, including 19 842 (64·4%; 63·8–64·9; 44·1–80·2) surgical patients and 15 487 (41·5%; 41·0–42·0; 21·1–71·2) medical patients. Of the surgical patients at risk, 11 613 (58·5%; 57·8–59·2; 0·2–92·1) received ACCP-recommended VTE prophylaxis, compared with 6119 (39·5%; 38·7–40·3; 3·1–70·4) at-risk medical patients.**

Interpretation **A large proportion of hospitalised patients are at risk for VTE, but there is a low rate of appropriate prophylaxis. Our data reinforce the rationale for the use of hospital-wide strategies to assess patients' VTE risk and to implement measures that ensure that at-risk patients receive appropriate prophylaxis.**

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Introduction

Venous thromboembolism (VTE) is a common complication during and after hospitalisation for acute medical illness or surgery. Pulmonary embolism accounts for 5–10% of deaths in hospitalised patients, making VTE the most common preventable cause of in-hospital death.[1–4] In addition to the acute risk of mortality, VTE is associated with long-term risks of post-thrombotic syndrome[5] and chronic thromboembolic pulmonary hypertension.[6] These complications contribute substantially to patient morbidity and the cost of management.

Evidence-based consensus guidelines for VTE prophylaxis have been available for more than 15 years.[7] Despite the existence of these guidelines, VTE prophylaxis remains underused.[8,9] Existing studies have assessed compliance with prophylaxis guidelines within defined institutions or countries,[8,10–12] but to date, the proportion of at-risk patients who should receive prophylaxis globally remains unknown.

We did the multinational, observational, cross-sectional Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care Setting (ENDORSE) study, a chart audit of medical and surgical patients in a large sample of hospitals worldwide. The study was designed to assess the number of patients at risk for VTE in the acute care hospital setting and to determine the proportion of these at-risk patients who received prophylaxis as recommended by the American College of Chest Physicians (ACCP) evidence-based consensus guidelines.[1]

Methods

Procedures

Hospitals were considered eligible for enrolment if they contained more than 50 beds, admitted patients for the treatment of medical illnesses and exacerbations of chronic diseases, and scheduled routine major surgical procedures. Non-acute and single specialty hospitals were excluded.

Hospitals were selected at random from authoritative lists of acute care hospitals in 32 participating countries. In the USA, a list of acute care hospitals from the American Hospital Association was used.[13] The European Hospital Register was used to identify eligible hospitals in major European countries.[14] For other countries, equivalent lists were obtained from the respective national hospital association or government health authorities. The study coordinating centre provided lists of randomly selected hospitals to the principal investigators, who contacted the hospital director at each site. Random number tables were used to select the sample of study hospitals by use of SAS version 9.1.

Panel: Types of venous thromboembolism prophylaxis

- Any anticoagulant—Any of the following types of prophylaxis used during hospitalisation: low-molecular-weight heparin; unfractionated heparin; vitamin K antagonist; fondaparinux; other anticoagulants given for protection against venous thromboembolism
- Intermittent pneumatic compression without anticoagulant
- Graduated compression stockings without any anticoagulants or intermittent pneumatic compression
- Antiplatelet agents (eg, aspirin) given for prevention of deep vein thrombosis or pulmonary embolism without anticoagulants, intermittent pneumatic compression, or graduated compression stockings
- None—None of the above

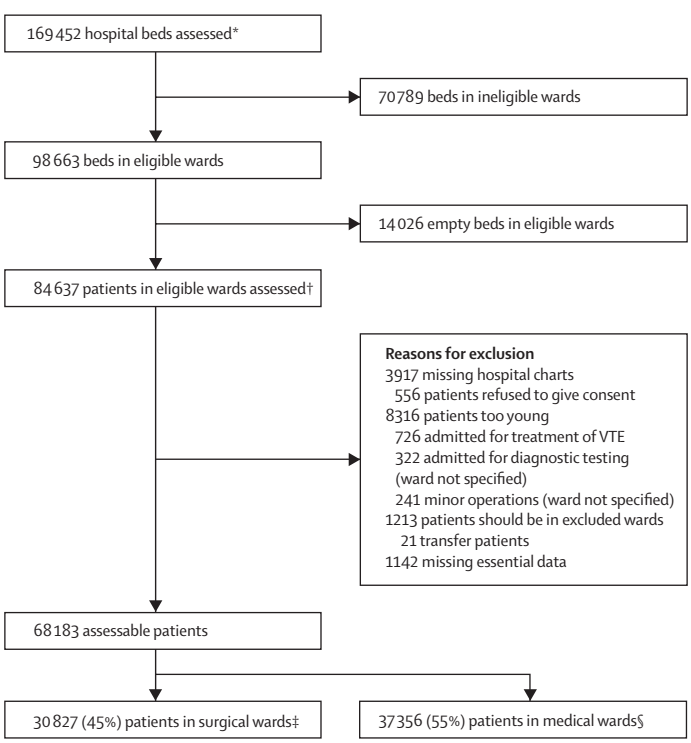

Figure 1: **Selection of study population and reasons for exclusion**
VTE=venous thromboembolism. *On basis of hospital enrolment forms. †On basis of patient enrolment logs, includes patients who did not meet protocol requirements (eg, age, type of condition, or missing hospital chart). ‡Includes patients in general surgical units, surgical intensive-care units, neurosurgery, gynaecology, and orthopaedics. §Includes patients in other eligible wards.

See Online for webtables 1 and 2

However, in Algeria, Bangladesh, Brazil, Bulgaria, Egypt, India, Pakistan, Russia, and Thailand, the feasibility of data collection in some randomly selected hospitals was thought to be impossible by the principal investigator because of the limited experience and capabilities for data collection in smaller, mainly non-academic hospitals. Therefore, study sites in these countries were individually selected from the list of eligible hospitals. Ethics committee approval to undertake the survey was obtained for hospitals in each country, in accordance with national and local regulations. Signed patient consent was required in Brazil, Greece, and Hungary.

Hospital wards were eligible if they were occupied by acute medical and surgical patients (eg, general medical, respiratory, or cardiac wards, and general surgical and orthopaedic wards). Psychiatric, paediatric, eye, ear, nose and throat, dermatology, alcohol/drug treatment, rehabilitation, accident and emergency, maternity, chronic, and palliative care wards were excluded. A study log was completed for each ward on the day of the survey, including non-selected wards, empty beds, and ineligible patients. All eligible wards within enrolled hospitals were included in the study.

Data were collected from a review of hospital charts on standard case report forms by trained data abstractors, who included physicians, nurses, and other hospital staff. A study protocol and training manual were provided to each investigator and data abstractor. The study documents were translated into 15 languages. Staff from the study coordinating centre travelled to each country to give 1-day training sessions for study coordinators and investigators. Because the typical hospital was too large to allow data abstractors to complete all patient enrolments in 1 day, investigators were asked to organise the data abstraction to complete at least one floor or ward on any particular day. Each ward was assessed on one pre-specified day to allow complete and systematic processing of patient data. For inclusion, each patient had to be an inpatient in an eligible ward on the day it was surveyed.

Data abstraction from all eligible charts in selected wards at each hospital was completed within 14 days and included patient demographics, admission and post-admission diagnoses, risk factors associated with VTE (defined in the ACCP guidelines[1]), risk factors for bleeding, duration of stay, and type of VTE prophylaxis (defined in the ACCP guidelines[1]).

Patients

Patients aged 40 years or more in eligible medical wards or 18 years or more in eligible surgical wards were screened. Patients were ineligible or excluded from the study if their chart was unavailable, they would normally have been admitted to an ineligible ward, were admitted solely for the treatment of VTE, or if they refused consent in countries where consent was necessary.

Enrolled patients were assessed for risk for VTE in accordance with the 2004 ACCP guidelines (webtables 1 and 2),[1] which included acutely ill medical patients and those admitted for major trauma or undergoing a major surgical procedure requiring general or epidural anaesthesia for at least 45 min.[1,15] Surgical patients were first assessed for age, type of surgery, and duration of anaesthesia, and then classified as being at highest, high, moderate, or low risk for VTE as per the ACCP guidelines.[1]

The use of recommended types of VTE prophylaxis received by at-risk patients was defined according to specific recommendations from the 2004 ACCP guidelines for the different types of patients at risk (panel).[1] When assessing whether prophylaxis was compliant with the ACCP guideline recommendations,[1] only the type of prophylaxis was considered. Data regarding the dose administered were collected; however, such data are not presented because of different dosing recommendations in different countries and because of variations in the drugs approved in different countries; furthermore, the ACCP does not give global recommendations for dosing schedules. Duration of dose could not be assessed because of the cross-sectional nature of this study.

Patients were considered to have a sufficient risk for bleeding to present a contraindication to anticoagulant prophylaxis if they presented with, or developed during hospitalisation, any of the following: intracranial haemorrhage; hepatic impairment; bleeding at hospital admission; active gastroduodenal ulcer; or a known bleeding disorder.[16]

Statistical analysis

Quantitative data were summarised as median (IQR) and the number of non-missing data. Categorical data were summarised into number and percentage of the population. Summary data are reported globally and by country. Global and country rates were calculated from individual patient data. To assess the true occurrence of VTE risk at 25% with a margin of error of 4%, a minimum of 450 patients per analysis group are required. 95% CI and between-country ranges were calculated for the main outcomes.

SAS version 9.1 was used for all statistical analyses.

Role of the funding source

The protocol was written by an independent scientific steering committee and revised after discussion with the study sponsor. Data collection was co-ordinated by the Center for Outcomes Research (University of Massachusetts Medical School, Worcester, MA, USA). All statistical analyses were done by the Center for Outcomes Research. All members of the steering committee had full access to all the data and were responsible for interpretation of the data, drafting and critical revision of the manuscript, and the decision to submit for publication.

Results

Between August, 2006, and January, 2007, eligible patients were enrolled from 358 hospitals across 32 countries that had completed the study within specified deadlines (Algeria, Australia, Bangladesh, Brazil, Bulgaria, Colombia, Czech Republic, Egypt, France, Germany, Greece, Hungary, India, Ireland, Kuwait, Mexico, Pakistan, Poland, Portugal, Romania, Russia, Saudi Arabia, Slovakia, Spain, Switzerland, Thailand, Tunisia, Turkey, United Arab Emirates, UK, USA, and Venezuela) in six continents.

	Met VTE risk criteria*	Did not meet VTE risk criteria*
Medical patients (15 487 met criteria, 21 869 did not)		
Sex (female)	7142/15 249 (47%)	10 430/20 504 (51%)
Age (years)	70·0 (58·0–79·0)	66·0 (54·0–76·0)
Length of hospitalisation up to survey date (days)	6·0 (2·0–11·0)	5·0 (2·0–10·0)
Body-mass index (kg/m²)	26·0 (22·7–30·4)	25·9 (22·8–29·7)
Reason for hospitalisation	N=15 487	N=20 864
Acute heart failure (NYHA class III or IV)	3259 (21%)	0† (0%)
Other cardiovascular disease	5310 (34%)	5524† (26%)
Acute non-infectious respiratory disease	2984 (19%)	0† (0%)
Pulmonary infection	4834 (31%)	0† (0%)
Infection (non-respiratory)	2298 (15%)	2272† (11%)
Ischaemic stroke	1649 (11%)	774† (4%)
Haemorrhagic stroke	402 (3%)	126† (0·6%)
Malignancy (active)	1072 (7%)	2041† (10%)
Rheumatological or inflammatory disease	714 (5%)	874† (4%)
Haematological diseases	796 (5%)	1229† (6%)
Neurological disease	1460 (9%)	2482† (12%)
Renal disease	1768 (11%)	1867† (9%)
Endocrine/metabolic disease	2593 (17%)	3236† (16%)
Gastrointestinal/hepatobiliary disease	1732 (11%)	3827† (18%)
Other medical conditions	1907 (12%)	2814† (13%)
Surgical patients (19 842 patients met criteria, 10 985 did not)		
Sex (female)	9249/19 499 (47%)	4313/8840 (49%)
Age (years)	60·0 (47·0–73·0)	55·0 (39·0–70·0)
Length of hospitalisation up to survey date (days)	6·0 (3·0–13·0)	3·0 (1·0–8·0)
Body-mass index (kg/m²)	26·2 (23·4–30·1)	25·4 (22·5–29·3)
Reason for hospitalisation	N=19 842	N=8999
Hip replacement	910 (5%)	0† (0%)
Knee replacement	634 (3%)	0† (0%)
Hip fracture	756 (4%)	0† (0%)
Curative arthroscopy	138 (0·7%)	33† (0·4%)
Other orthopaedic trauma	2052 (10%)	95† (1%)
Gastric surgery	680 (3%)	51† (0·6%)
Hepatobiliary surgery	1099 (6%)	123† (1%)
Colon/small bowel surgery	1668 (8%)	289† (3%)
Rectosigmoid surgery	381 (2%)	21† (0·2%)
Urological surgery	1408 (7%)	90† (1%)
Gynaecological surgery	936 (5%)	219† (2%)
Thoracic surgery	699 (4%)	17† (0·2%)
Vascular surgery	1012 (5%)	26† (0·3%)
Other surgery	4711 (24%)	413† (5%)
Admitted with major trauma but surgery not done	2758 (14%)	0† (0%)
Under observation in surgical wards	0 (0%)	4483† (50%)
Awaiting elective surgery	0 (0%)	3139† (35%)

Data are median (IQR), n (%), or n/N (%). NYHA=New York Heart Association. VTE=venous thromboembolism. Denominator varies for different data categories due to missing hospital charts. *Percentages might add to more than 100% because patients can have more than one medical condition. †Primary diagnosis data not available for all patients who did not meet inclusion criteria.

Table 1: **Characteristics and reasons for hospitalisation of assessable patients**

Of the 340 hospitals who provided characteristic data, 149 (44%) were categorised as academic (range across participating countries 17–100%). The median number of beds per hospital was 352 (range across participating countries 169–1120 beds). The size of participating hospitals was comparable with the overall median size of hospitals within a given country.[13,14] The number of beds assessed, and reasons for exclusion from assessment, are shown in figure 1, together with the number of assessable medical and surgical patients. Median time to identify and enrol eligible patients within a hospital was 8 (IQR 2–14) days.

Reasons for hospital admission and general characteristics of the patients are shown in table 1. Of the patients in medical wards, median age was 67 (IQR 56–78) years, median body-mass index (BMI) was 26 (22·8–30·0) kg/m², and 17 272 (49%) were women. The median age of patients in surgical wards was 59 (45–72) years, median BMI was 26 (23·1–30·0) kg/m², and 13 562 (48%) were women. Median length of hospital stay up to the survey date was 5·0 (2·0–11·0) days in the overall study population, 5·0 (2·0–10·0) days for patients in medical wards, and 5·0 (2·0–12·0) days for those in surgical wards.

35 329 (51·8%; 95% CI 51·4–52·2; range 35·6–72·6) of the enrolled patients were deemed to be at risk for VTE. 19 842 (64·4%; 63·8–64·9; 44·1–80·2) surgical patients were at risk, as were 15 487 (41·5%; 41·0–42·0; 21·1–71·2) patients in the medical population.

Risk factors for VTE that were present before admission are shown in table 2. Of the patients with such risk factors before admission, 16 391 (47%) were women; median age was 65 (IQR 52–76) years. In medical patients, the most common VTE risk factors before hospitalisation were chronic pulmonary disease and chronic heart failure, whereas obesity was the main risk factor present before hospitalisation in surgical patients. The most common post-admission risk factors for VTE in both medical and surgical patients were complete immobilisation, immobilisation with bathroom privileges, and admission to an intensive or critical care unit (table 2).

The most common contraindications to pharmacological prophylaxis in medical patients were bleeding on admission and clinically relevant hepatic impairment (table 3). In surgical patients, bleeding at hospital admission and intracranial bleeding were the most common contraindications (table 3). Of the population at risk for VTE, 1549 (10%) medical patients and 1791 (9%) surgical patients were considered to have a high bleeding risk, sufficient to present a contraindication to anticoagulant prophylaxis.

17 732 (50·2%; 95% CI 49·7–50·7; range 1·6–84·2) patients deemed to be at risk for VTE received ACCP-recommended types of prophylaxis, of whom 11 613 (58·5%; 57·8–59·2; 0·2–92·1) were surgical patients and 6119 (39·5%; 38·7–40·3; 3·1–70·4) were medical patients. The proportion of patients receiving ACCP-recommended prophylaxis varied between patients undergoing different types of surgery—eg, 88% of patients undergoing hip or knee replacement were receiving prophylaxis, compared with 69% of those undergoing colorectal surgery, and 50% of those undergoing urological surgery. Additionally, 474 (34%) of 1377 surgical patients classified as being at low risk for VTE received prophylaxis. The proportion of at-risk

	Medical patients	Surgical patients	Overall
Before admission			
N	15 253*	18 544*	33 797*
Previous venous thromboembolism	750 (5%)	466 (3%)	1216 (4%)
Obesity	1744 (11%)	1875 (10%)	3619 (11%)
Varicose veins or venous insufficiency	1010 (7%)	1308 (7%)	2318 (7%)
Thrombophilia	73 (0·5%)	48 (0·3%)	121 (0·4%)
Post-menopausal hormone replacement therapy	61 (0·4%)	143 (0·8%)	204 (0·6%)
Chronic pulmonary disease	4087 (27%)	1555 (8%)	5642 (17%)
Long term immobility	1181 (8%)	474 (3%)	1655 (5%)
Pregnancy (within 3 months)	9 (0·1%)	59 (0·3%)	68 (0·2%)
Contraceptives	37 (0·2%)	158 (0·9%)	195 (0·6%)
Chronic heart failure	3749 (25%)	1585 (9%)	5334 (16%)
During hospitalisation			
N	15 487	19 842	35 329
Admitted to intensive care unit/critical care unit	4389 (28%)	4595 (23%)	8984 (25%)
Central venous catheter	1751 (11%)	3110 (16%)	4861 (14%)
Mechanical ventilation	1278 (8%)	2448 (12%)	3726 (11%)
Immobile with bathroom privileges	4303 (28%)	4621 (23%)	8924 (25%)
Complete immobilisation	5132 (33%)	7797 (39%)	12 929 (37%)
Cancer therapy	277 (2%)	108 (0·5%)	385 (1%)
Heparin-induced thrombocytopenia	29 (0·2%)	25 (0·1%)	54 (0·2%)

Data are n (%). *Data on pre-admission risk factors for VTE unavailable for some medical and surgical patients.

Table 2: **Risk factors for venous thromboembolism**

	Medical patients N=15 487	Surgical patients N=19 842	Overall N=35 329
Significant renal impairment	1657 (11%)	902 (5%)	2559 (7%)
Low platelet count (<100 000 per µL)	572 (4%)	282 (1%)	854 (2%)
Aspirin use	4625 (30%)	2283 (12%)	6908 (20%)
NSAID use (excluding aspirin)	962 (6%)	2665 (13%)	3627 (10%)
Intracranial haemorrhage*†	255 (2%)	519 (3%)	774 (2%)
Known bleeding disorder (congenital or acquired)†	148 (1%)	88 (0·4%)	236 (0·7%)
Clincally relevant hepatic impairment†	518 (3%)	337 (2%)	855 (2%)
Bleeding at hospital admission†	571 (4%)	1052 (5%)	1623 (5%)
Active gastroduodenal ulcer†	283 (2%)	218 (1%)	501 (1%)

Data are n (%). *528 patients with haemorrhagic stroke diagnosed at admission or after admission included. 402 met the VTE risk criteria, 126 did not meet the criteria, mainly because of not being immobile. 255 diagnosed at admission and defined as having a contraindication to anticoagulation because of an intracranial haemorrhage. 147 diagnosed post-admission. †Absolute contraindications, defined in accordance with Baglin and colleagues.[16]

Table 3: **Contraindications to anticoagulation**

medical patients receiving prophylaxis was generally lower than that in surgical patients, ranging from 37% in patients with active malignancy or ischaemic stroke to 45% of patients with acute non-infectious respiratory disease. 6105 (29%) medical patients who were at low risk for VTE received prophylaxis.

Anticoagulants were the most frequently used form of VTE prophylaxis in the at-risk population; low-molecular-weight heparin was the most commonly prescribed anticoagulant (table 4). All types of mechanical prophylaxis (foot pump, graduated compression stockings, and intermittent pneumatic compression) were used more frequently in surgical patients than in medical patients (table 4). Of the patients deemed to be contraindicated to anticoagulant prophylaxis due to a high risk of bleeding, 139 (8%) surgical and 106 (7%) medical patients received intermittent pneumatic compression alone, and 87 (5%) surgical and 54 (3%) medical patients received graduated compression stockings alone.

The proportion of patients at risk for VTE and the use of ACCP-recommended prophylaxis by country are shown in figure 2. Worldwide, the proportion of hospital patients at risk for VTE ranged among countries from 36% to 73% and the proportion of patients receiving ACCP-recommended prophylaxis ranged from 2% to 84%. The proportion of medical patients at risk for VTE ranged among countries from 21% to 71%, for surgical patients the range was from 44% to 80% (table 5). The use of recommended VTE prophylaxis in medical patients varied from 3% to 70% between countries and for surgical patients between 0·2% and 92% (table 5).

Discussion

The data gathered show that, worldwide, more than half of all hospitalised patients are at risk for VTE, and that surgical patients seem to be at higher risk than are medical patients. Furthermore, only half of at-risk patients received an ACCP-recommended method of prophylaxis. Previous studies have reported overall VTE prophylaxis rates ranging from 13% to 64%.[8–12] This variability is largely due to individual studies limiting their assessment to predefined populations (eg, orthopaedic surgery patients) and the substantial differences that can exist between institutions within a country, as shown by Otero and colleagues,[8] who reported prophylaxis rates of 27–70% across different hospitals in Spain.

The proportion of patients at risk for VTE did not vary greatly from country to country. However, there were marked differences between countries in the frequency of use of ACCP-recommended types of prophylaxis,[1,17,18] which could be due to many factors, including physician awareness, availability of guidelines, education factors, reimbursement, and national health-care resources.

The use of recommended VTE prophylaxis was particularly poor in medical patients, with prophylaxis received by only 37% of patients with active malignancy and ischaemic stroke—two of the highest risk groups for VTE. This finding is consistent with other studies that have shown low use of prophylaxis in at-risk

	Medical patients (N=15 487)	Surgical patients (N=19 842)	Overall (N=35 329)
Any anticoagulant	6596 (43%)	10 901 (55%)	17 497 (50%)
Intermittent pneumatic compression without anticoagulant	318 (2%)	880 (4%)	1198 (3%)
Graduated compression stockings without an anticoagulant or intermittent pneumatic compression	291 (2%)	745 (4%)	1036 (3%)
Aspirin for prophylaxis without anticoagulant/ intermittent pneumatic compression/elastic stockings	214 (1%)	83 (0·4%)	297 (0·8%)
None	8068 (52%)	7233 (36%)	15 301 (43%)
Low-molecular-weight heparin	4667 (30%)	9204 (46%)	13 871 (39%)
Unfractionated heparin	1454 (9%)	1564 (8%)	3018 (9%)
Vitamin K antagonist	694 (4%)	483 (2%)	1177 (3%)
Fondaparinux	9 (0·1%)	39 (0·2%)	48 (0·1%)
Other anticoagulants	308 (2%)	252 (1%)	560 (2%)
Intermittent pneumatic compression	564 (4%)	1949 (10%)	2513 (7%)
Foot pump	41 (0·3%)	338 (2%)	379 (1%)
Graduated compression stockings	777 (5%)	3677 (19%)	4454 (13%)

Data are n (%).

Table 4: **Type of prophylaxis used in at-risk patients**

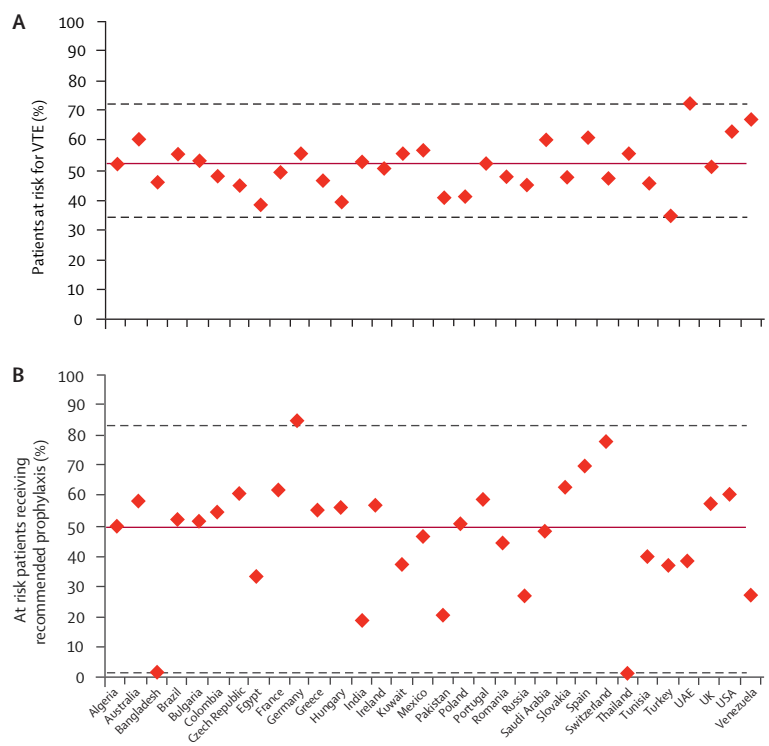

Figure 2: **Proportion of patients at risk for VTE (A) and proportion of at-risk patients receiving recommended prophylaxis (B)**

	Assessable medical patients	At-risk medical patients	At-risk medical patients receiving any prophylaxis	At-risk medical patients receiving ACCP-recommended prophylaxis*	Assessable surgical patients	At-risk surgical patients	At-risk surgical patients receiving any prophylaxis	At-risk surgical patients receiving ACCP-recommended prophylaxis*
Algeria	440	200 (46%)	62 (31%)	53 (27%)	446	265 (59%)	183 (69%)	183 (69%)
Australia	834	406 (49%)	208 (51%)	172 (42%)	496	398 (80%)	325 (82%)	287 (72%)
Bangladesh	1081	483 (45%)	24 (5%)	15 (3%)	962	465 (48%)	2 (0·4%)	1 (0·2%)
Brazil	655	299 (46%)	181 (61%)	176 (59%)	640	421 (66%)	214 (51%)	192 (46%)
Bulgaria	1477	611 (41%)	285 (47%)	194 (32%)	1333	906 (68%)	621 (69%)	598 (66%)
Colombia	543	215 (40%)	137 (64%)	137 (64%)	218	157 (72%)	76 (48%)	67 (43%)
Czech Republic	1389	478 (34%)	259 (54%)	210 (44%)	945	591 (63%)	498 (84%)	437 (74%)
Egypt	530	168 (32%)	63 (38%)	55 (33%)	478	227 (47%)	86 (38%)	80 (35%)
France	1927	701 (36%)	432 (62%)	375 (53%)	917	718 (78%)	542 (75%)	511 (71%)
Germany	1160	479 (41%)	370 (77%)	337 (70%)	1210	838 (69%)	790 (94%)	772 (92%)
Greece	898	347 (39%)	133 (38%)	113 (33%)	947	525 (55%)	390 (74%)	376 (72%)
Hungary	865	266 (31%)	86 (32%)	75 (28%)	435	253 (58%)	220 (87%)	219 (87%)
India	948	424 (45%)	95 (22%)	81 (19%)	1110	680 (61%)	126 (19%)	111 (16%)
Ireland	255	109 (43%)	55 (50%)	51 (47%)	297	175 (59%)	142 (81%)	112 (64%)
Kuwait	324	197 (61%)	73 (37%)	66 (34%)	161	74 (46%)	45 (61%)	43 (58%)
Mexico	307	118 (38%)	80 (68%)	61 (52%)	531	362 (68%)	193 (53%)	154 (43%)
Pakistan	565	213 (38%)	86 (40%)	70 (33%)	748	330 (44%)	46 (14%)	33 (10%)
Poland	1581	514 (33%)	239 (46%)	179 (35%)	1092	597 (55%)	404 (68%)	396 (66%)
Portugal	870	335 (39%)	205 (61%)	193 (58%)	762	525 (69%)	319 (61%)	310 (59%)
Romania	3272	1168 (36%)	284 (24%)	213 (18%)	2461	1609 (65%)	1019 (63%)	1011 (63%)
Russia	1959	718 (37%)	159 (22%)	141 (20%)	2829	1470 (52%)	487 (33%)	380 (26%)
Saudi Arabia	154	92 (60%)	61 (66%)	57 (62%)	313	192 (61%)	132 (69%)	62 (32%)
Slovakia	1260	462 (37%)	280 (61%)	217 (47%)	1003	636 (63%)	517 (81%)	487 (77%)
Spain	2069	1140 (55%)	803 (70%)	731 (64%)	996	738 (74%)	612 (83%)	605 (82%)
Switzerland	847	179 (21%)	144 (80%)	109 (61%)	1153	780 (68%)	663 (85%)	631 (81%)
Thailand	823	406 (49%)	15 (4%)	15 (4%)	1001	618 (62%)	4 (0.6%)	1 (0.2%)
Tunisia	673	313 (47%)	95 (30%)	92 (29%)	212	95 (45%)	75 (79%)	74 (78%)
Turkey	1211	288 (24%)	113 (39%)	111 (39%)	490	318 (65%)	126 (40%)	124 (39%)
United Arab Emirates	170	121 (71%)	49 (40%)	40 (33%)	169	125 (74%)	57 (46%)	54 (43%)
UK	2751	1123 (41%)	509 (45%)	414 (37%)	2091	1350 (65%)	1095 (81%)	1003 (74%)
USA	5196	2720 (52%)	1752 (64%)	1292 (48%)	4061	3165 (78%)	2543 (80%)	2244 (71%)
Venezuela	322	194 (60%)	82 (42%)	74 (38%)	320	239 (75%)	57 (24%)	55 (23%)
Total	37 356	15 487 (42%)	7419 (48%)	6119 (40%)	30 827	19 842 (64%)	12 609 (64%)	11 613 (59%)

Data are N or n (%). *When assessing whether prophylaxis was compliant with the ACCP recommendations, only the type of prophylaxis was considered.

Table 5: **Patients at risk for VTE and prophylaxis use by country**

medical patients.[12,19] In surgical patients, prophylaxis rates were generally higher, although the proportion of patients receiving prophylaxis varied with type of surgery.

The increased use of prophylaxis in the surgical setting compared with the medical setting could result from several factors. First, the benefits of prophylaxis in the surgical setting have been accepted for many years,[16] while trials in medical patients have been more recent and physician awareness for VTE risk is lower in this population.[1] Second, assessment of VTE risk in surgical patients is simpler than in medical patients, the principal criteria being the type of surgery rather than a range of illnesses and risk factors as presented in medical patients. Even in countries where prophylaxis is commonly provided to at-risk patients, we noted that rates of prophylaxis were low in medical patients with high-risk conditions such as congestive heart failure.[20,21]

The low use of prophylaxis in medical patients has been seen in other studies. In the IMPROVE study,[12] a multinational observation study of 15156 acutely ill medical patients, 60% of patients judged to be at risk of VTE actually received prophylaxis. This rate is somewhat higher than recorded here, possibly because IMPROVE had a broader definition of prophylaxis and the patients were mainly from academic centres experienced in doing clinical trials of VTE prevention. In the CURVE study,[19] a chart audit in 29 Canadian hospitals, 90% of acutely ill medical patients had an indication for thrombo-

prophylaxis. However, only 16% received appropriate prophylaxis (defined as an ACCP-recommended type of prophylaxis administered at the approved Canadian dose). The very high hospital frequency of medical patients at risk for VTE makes it difficult to compare with ENDORSE.

Patients' bleeding risk also has a role in the decision to provide appropriate VTE prophylaxis and could lead to the use of mechanical thromboprophylaxis rather than anticoagulants. Of surgical and medical patients at risk for VTE, 10% were classified as being at high risk for bleeding. However, the low use of VTE prophylaxis cannot be accounted for solely because of relative or absolute contraindications to anticoagulant prophylaxis, because these patients could have received ACCP-recommended forms of mechanical prophylaxis.

The trial information, data forms, and training were identical, including translation of key study documents into 15 languages, allowing standard methodology to be applied. The assessment of patients on any particular ward, on a pre-specified day, allowed complete and systematic processing of patient information by trained data abstractors, which further improved the data quality.

The 2004 ACCP guidelines were used to define the at-risk population and effective types of prophylaxis.[1] Although other standards could have been applied, such as the International Consensus Statement,[17] the 2004 ACCP recommendations were adopted as the best established and most widely referenced standard, and have been used in other studies of VTE prophylaxis.[9,11]

This study has several potential limitations. ENDORSE might not be representative of non-participating countries. However, our study did include 32 countries from six continents with a wide range of ethnic, social, economic, and health-care environments. The data were captured from patient charts rather than from interviews, which could have led to some inaccuracies and failure to capture the most recent information. However, this approach generally eliminated the need for patient consent and therefore allowed the most representative sampling of hospital patients, since all eligible ward patients were enrolled, including those unable to give a medical history. Because this study was cross-sectional by design, we were only able to assess the quality of treatment up to the date of this survey. For most patients, we were unable to assess the duration of adherence with prophylaxis throughout the full hospital stay, which might have resulted in an overestimation of rates of appropriate VTE prophylaxis. Errors could also have been introduced when data were recorded. However, even if some of the original diagnoses were incorrect, such mistakes could have been corrected by the time our survey occurred.

The ACCP defines patients at risk for VTE, but this does not mean that medical and surgical patients who do not meet these criteria are not at risk, or that providing thromboprophylaxis to these patients is inappropriate. Accordingly, physicians could differ in their opinions about the need for, and benefit of, prophylaxis in some patient groups that were not defined as at risk for VTE in the present study. These differences are understandable because many major surgical operations and severe medical conditions have never been studied in well-designed clinical trials. Another potential limitation of this study is that although we defined and collected information on standard bleeding risks, some physicians could have applied broader interpretations and withheld VTE prophylaxis accordingly. Additionally, we collected information only on factors that affected the initiation of anticoagulant prophylaxis and not the factors resulting in the delaying, changing, or stopping of prophylaxis. A further limitation is that, although some major trauma patients might be contraindicated to anticoagulant prophylaxis, leg injuries could have precluded the use of mechanical prophylaxis. Given there were few major trauma cases included in this study, this limitation is unlikely to have affected the main conclusions. Lastly, we cannot rule out that physicians became aware of this study and altered their behaviour, although the one-ward, one-day strategy was designed to minimise this source of bias. Clearly, patient risk could not have been altered by physician knowledge of this survey. Furthermore, the data still show a large gap between ideal and real-world practices, despite the theoretical possibility that physician awareness might have led to increased use of VTE prophylaxis.

Our data are important from national health-care perspectives, since they allow estimation of both the patient welfare and economic benefits of fully applying evidence-based VTE prophylaxis. Although several studies have shown that gaps exist between evidence-based guidelines and recommendations and practice in the hospital setting,[8,10] the absence of a global overview of this problem could have represented a barrier to physicians uncertain of the prevalence of VTE risk in the patients they manage.

VTE is a major public health issue:[22,23] it is an easily preventable disease with a substantial risk of morbidity and mortality in patients hospitalised for acute medical and surgical illnesses.[1,15] Our data show that, globally, a large proportion of hospitalised individuals—both surgical and medical—are at risk for VTE, and that recommended VTE prophylaxis is underused. Hospital-wide strategies to assess patients' VTE risk should be implemented, together with measures that ensure that at-risk patients receive appropriate VTE prophylaxis.

Contributors

All authors participated in the study design, interpretation of results, and writing, critically reviewing, or revising the report. All authors saw and approved the final version of the manuscript report, and were fully responsible for content and editorial decisions.

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Conflict of interest statement

ATC, VFT, JFB, SZG, AKK, and FAA were members of the ENDORSE steering committee. ATC has received consultancy fees and clinical research funding from AstraZeneca, Bayer, Boehringer-Ingelheim, BMS, Daiichi, GSK, Johnson & Johnson, Mitsubishi Pharma, Organon, Pfizer, sanofi-aventis, Schering Plough, and Takeda. VFT has received consultancy fees and clinical research funding from Bayer and sanofi-aventis. JFB discloses consultancy for AstraZeneca and GSK. SZG has received funding from Bayer, Boehringer-Ingelheim, BMS, Eisai, Emisphere, and sanofi-aventis for consultancy and clinical research. AKK has received honoraria from sanofi-aventis for participation in the ENDORSE study, consultancy fees from BMS, Boehringer-Ingelheim, Daiichi, Eisai, Johnson & Johnson, Pfizer and sanofi-aventis, and research funding from Boehringer-Ingelheim, Eisai and sanofi-aventis. BD is an employee of sanofi-aventis. WH, MZ, LE, and FAA are employees at the Center for Outcomes Research, which receives research grants from sanofi-aventis and The Medicines Company. FAA has received speaker honoraria and consulting contracts from sanofi-aventis, The Medicines Company, Millennium Pharmaceuticals, GSK and Johnson & Johnson.

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